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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/892,227	06/25/2001	Hermann Bujard	BBI-013C2CN2	7548

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EXAMINER	
PARAS JR, PETER	

ART UNIT	PAPER NUMBER
1632	

DATE MAILED: 03/15/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/892,227	BUJARD ET AL.	
	Examiner	Art Unit	
	Peter Paras, Jr.	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 January 2004 and 17 September 2003*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *23-40* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *23-40* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Applicant's amendments received on 9/17/03 and 1/8/04 have been entered. Claims 23 and 33-35 have been amended. Claims 23-40 are pending and are under current consideration.

Claim Rejections - 35 USC § 112, 1st paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 23-40 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the claimed invention to the extent of a transgenic mouse, does not reasonably provide enablement for all other transgenic non-human animals embraced by the claims. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims. The previous rejection is maintained for the reasons of record advanced on pages 3-10 of the Office action mailed on 6/17/03.

Applicant's arguments filed 9/17/03 have been fully considered but they are not persuasive. Applicants argue the tTA system described is a highly regulated transcriptional system which works with endogenous transcriptional machinery to directly or indirectly activate transcription of a gene of interest through the activity of an effector molecule, Tc, binding to a TetR activator fusion. Applicant clarify that

transcription does not occur with the TetR-activator fusion alone. Rather, Applicants continue to argue the tet regulatory system embraced by the claims provides a reliable and predictable method of controlling gene expression in a transgenic non-human animal because such a system does not rely on endogenous transcriptional activators and/or inhibitors. See page 9 of the amendment.

In response, the Examiner asserts the Applicant's arguments are off-point with respect to addressing the position effect as discussed by Wall. See pages 4-5 of the Office action mailed on 6/17/03. Since it is clear the tTA system *works with endogenous transcriptional machinery* to directly or indirectly activate transcription of a gene of interest Applicant's arguments with respect to transcription are not germane to a discussion regarding position effect of transgene integration. Applicants have not addressed why or how the tTA system overcomes the position effect since endogenous transcriptional machinery is needed. A suggestion the position effect is overcome because the tTA system does not require an endogenous transcriptional activator or inhibitor is not sufficient.

Applicants argue the methodologies taught in the instant specification as well as general knowledge in the art fully support the breadth of the claims directed to non-human animals. Applicants argue that transgenic non-human animals other than mice had been created at the time of filling. Applicants refer to previously submitted references (Pursel, Rexroad, and Ebert) and to newly submitted references (WO 92/22646, WO 93/25017, US 5,366,894, Fodor et al, Kroshus, Wall, and WO 97/19589)

in support of their assertions the claims are enabled for all species of transgenic animals. See pages 10-11 of the amendment.

In response, the Examiner maintains the instant specification has not provided guidance correlating to the production of transgenic non-human animals other than mice. The Examiner asserts that the issue is not whether or not transgenic non-human animals other than mice can be created as argued by Applicants. The issue is whether expression of a tet operator-linked gene will produce a reproducible phenotype when expressed in different species of transgenic non-human animals. None of the cited references address this issue. A controllable system, such as tTA, cannot provide a correlation between expression of a gene of interest and a resulting detectable and functional phenotype in a transgenic non-human animal. It is further maintained that is not possible to predict a phenotype resulting from expression of the same transgene in different animals. The evidence of record has provided guidance that correlates to the production of a transgenic mouse comprising a tTA system. However, the evidence of record has not provided guidance that correlates to production of other transgenic non-human animals comprising a tTA system. Moreover, the evidence of record has not provided guidance that correlates a tTA system with the observation of the same phenotypes in different species of non-human animals. As such, the evidence of record has not provided adequate guidance to overcome the unpredictability of a phenotype resulting from expression of a transgene in different species of non-human animals. See Houdebine, Hammer, Ebert, Mullins, Kappel, and Strojek and Wagner as discussed on pages 5-8 of the Office action mailed on 6/17/03.

Applicants argue that merely routine experimentation is required to identify a transgenic non-human animal, of the claimed invention, having a desired phenotype. Applicants refer to Kroshus et al for support of their assertion that routine experimentation is required to identify a transgenic non-human animal having a desired phenotype.

In response, the Examiner maintains that the phenotype resulting from transgene expression in a transgenic non-human animal is unpredictable. It is further maintained that Wall and Houdebine teach that there are not any features of any given transgene construct that are correlatable to a predictable phenotype in a transgenic non-human animal. See above. Applicant's arguments are based on the premise that it only requires routine experimentation to screen for a transgenic non-human animal that exhibits a desired phenotype, wherein more transgenic non-human animals can be created in order to find one that exhibits the desired phenotype or an animal with the most desirable phenotype can be selected. However, the fact that more transgenic non-human animals would need to be created before one with the desired phenotype is found clearly suggests that the phenotype resulting from transgene expression is unpredictable. If the transgenic art is in fact predictable, as Applicants are attempting to argue, then why must there even be a screening or selection process to identify an animal with the desired phenotype. It is maintained there is no way to predict that an expected phenotype will result in any given transgenic non-human animal. See above.

Applicants have not addressed the additional rejection over claims 27-30 with respect to the availability of embryonic stem (ES) cells from non-human animal species other than mice.

As such, the Examiner maintains that ES cells from non-human animal species other than mice are not enabled. Therefore, it is maintained ES cell technology is limited to the mouse system. See pages 9-10 of the Office action mailed on 6/17/03.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 23-40 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-20 of U.S. Patent No. 5,859,310. The previous rejection is maintained for the reasons of record advanced on pages 11-12 of the Office action mailed on 6/17/03.

Applicants submit that a terminal disclaimer will filed upon indication the pending claims are allowable.

In response, the Examiner maintains the instant claims are unpatentable over claims 1-20 of U.S. Patent No. 5,859,310. See pages 11-12 of the Office action mailed on 6/17/03.

Conclusion

No claim is allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner(s) should be directed to Peter Paras, Jr., whose telephone number is (571) 272-0732. The examiner can normally be reached Monday-Friday from 8:30 to 4:30 (Eastern time).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Amy Nelson, can be reached at 571-272-0804. Papers related to this application may be submitted by facsimile transmission. Papers should be faxed via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Official Fax Center number is (703) 872-9306.

Inquiries of a general nature or relating to the status of the application should be directed to Dianiece Jacobs whose telephone number is (571) 272-0532.

Peter Paras, Jr.

Art Unit 1632

PETER PARAS, JR.
PRIMARY EXAMINER